

Listing of Claims

This listing of claims will replace all prior versions and listings of claims in the application.

Claims 1-23 (cancelled)

Claim 24. (currently amended) A method for screening a plurality of compounds so as to identify compounds exhibiting anxiolytic activity, comprising:

- a) determining *in vitro* efficacy and EC₅₀ value for each compound at an ~~$\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor~~ or an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;
- b) determining *in vitro* efficacy values for each compound at a GABA_A receptor comprised of an α_1 subunit or an α_5 subunit; and
- c) identifying as exhibiting anxiolytic activity each compound having an EC₅₀ value determined in a) of less than 200nM and an efficacy value measured in a) greater than the efficacy measured in b).

Claim 25. (original) The method of Claim 24 wherein the EC₅₀ measured in step a) is less than 150 nM.

Claim 26. (currently amended) The method of Claim 25 wherein the *in vitro* efficacy measured at said ~~$\alpha_2\beta_3\gamma_2$~~ or said $\alpha_3\beta_3\gamma_2$ GABA_A receptor is greater than 20%.

Claim 27. (currently amended) The method of Claim 25 wherein the *in vitro* efficacy measured at said ~~$\alpha_2\beta_3\gamma_2$~~ or said $\alpha_3\beta_3\gamma_2$ GABA_A receptor is greater than 30%.

Claim 28. (original) The method of Claim 27 wherein the *in vitro* efficacy measured at said GABA_A receptor comprised of said α_1 or said α_5 subunit is less than 20%.

Claim 29. (currently amended) The method of Claim 24 wherein the *in vitro* efficacy measured at said ~~$\alpha_2\beta_3\gamma_2$~~ or $\alpha_3\beta_3\gamma_2$ GABA_A receptor is greater than 20%.

Claim 30. (currently amended) The method of Claim 24 wherein the *in vitro* efficacy measured at said ~~$\alpha_2\beta_3\gamma_2$~~ or $\alpha_3\beta_3\gamma_2$ GABA_A receptor is greater than 30%.

Claim 31. (original) The method of Claim 30 wherein the *in vitro* efficacy measured at said GABA_A receptor comprised of said α_1 or said α_5 subunit is less than 20%.

Claim 32. (original) The method of Claim 24 wherein the GABA_A receptor comprised of said α_1 subunit is an $\alpha_1\beta_2\gamma_2$ GABA_A subtype receptor or the GABA_A receptor comprised of said α_5 subunit is an $\alpha_5\beta_3\gamma_2$ GABA_A subtype receptor.

Claim 33. (currently amended) A method for screening for compounds having anxiolytic activity, comprising:

- a) selecting a compound having a binding affinity less than 100 nM at any GABA_A receptor;
- b) measuring *in vitro* efficacy and EC₅₀ values for each compound at an ~~$\alpha_2\beta_3\gamma_2$~~ or $\alpha_3\beta_3\gamma_2$ GABA_A receptor;
- c) measuring *in vitro* efficacy values for each compound at a GABA_A receptor comprised of an α_1 or α_5 subunit; and
- d) selecting a compound having an EC₅₀ value measured in a) ~~or~~ b) of less than 200nM and an efficacy value measured in b) greater than the efficacy measured in c).

Claim 34. (currently amended) A method for screening compounds so as to select at least one compound having anxiolytic activity, comprising:

- a) measuring *in vitro* efficacy and EC₅₀ values for each compound at an ~~$\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor~~ or an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;
- b) measuring *in vitro* efficacy and ~~EC₅₀ values~~ for each compound at a GABA_A receptor comprised of an α_1 or α_5 subunit;
- c) measuring *in vivo* effects of each compound in an animal model indicative of anxiolytic activity;
- d) measuring *in vivo* effects of each compound in an animal model indicative of sedative effects; and
- e) selecting each compound having: an EC₅₀ value measured in a) of less than 200nM, an efficacy value measured in ~~b)~~ a) greater than the efficacy measured in step ~~e)~~ b), a statistically significant ($p < 0.05$) positive effect in the animal model indicative of anxiolytic activity, and no statistically significant effect in the animal indicative of sedative effects.

Claim 35. (currently amended) A method for screening a plurality of compounds so as to identify at least one compound having anxiolytic activity, comprising:

- a) selecting a compound having a binding affinity less than 100 nM at any GABA_A receptor;

- b) measuring *in vitro* efficacy and EC₅₀ values for each selected compound at an ~~$\alpha_2\beta_3\gamma_2$~~ or $\alpha_3\beta_3\gamma_2$ GABA_A receptor;
- c) measuring *in vitro* efficacy for each selected compound at a GABA_A receptor comprised of an α_1 or α_5 subunit;
- d) measuring *in vivo* effects of each selected compound in an animal model indicative of anxiolytic activity;
- e) measuring *in vivo* effect of each selected compound in an animal model indicative of sedative effects; and
- f) selecting a compound having: an EC₅₀ value measured in b) of less than 200nM, an efficacy measured in ~~e)~~ b) greater than the efficacy measured in ~~d)~~ c), a statistically significant (p < 0.05) positive effect in the animal model indicative of anxiolytic activity, and no statistically significant effect in the animal indicative of sedative effects.

Claims 36-50 (cancelled)

Claim 51. (new) The method of Claim 24, comprising:

- a) determining *in vitro* efficacy and EC₅₀ value for each compound at an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor and an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;

- b) determining *in vitro* efficacy values for each compound at a GABA_A receptor comprised of an α_1 subunit or an α_5 subunit; and
- c) identifying as exhibiting anxiolytic activity each compound having
- an EC₅₀ value at an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor of less than 200nM;
- an EC₅₀ value at an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor of less than 200nM;
- an efficacy value at an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor greater than the efficacy measured in b); and
- an efficacy value at an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor greater than the efficacy measured in b).

Claim 52. (new) The method of Claim 50 wherein the *in vitro* efficacy measured at said $\alpha_2\beta_3\gamma_2$ and said $\alpha_3\beta_3\gamma_2$ GABA_A receptor is greater than 20%.

- Claim 53. (new) The method of claim 33, comprising:
- a) selecting a compound having a binding affinity less than 100 nM at any GABA_A receptor;
- b) measuring *in vitro* efficacy and EC₅₀ values for each compound at an $\alpha_2\beta_3\gamma_2$ and an $\alpha_3\beta_3\gamma_2$ GABA_A receptor;

- c) measuring *in vitro* efficacy values for each compound at a GABA_A receptor comprised of an α_1 or α_5 subunit; and
- d) selecting a compound having EC₅₀ values measured in b) of less than 200nM and an efficacy values measured in b) greater than the efficacy measured in c).

Claim 54. (new) The method of claim 34, comprising:

- a) measuring *in vitro* efficacy and EC₅₀ values for each compound at an $\alpha_2\beta_3\gamma_2$ GABA_A subtype receptor and an $\alpha_3\beta_3\gamma_2$ GABA_A subtype receptor;
- b) measuring *in vitro* efficacy for each compound at a GABA_A receptor comprised of an α_1 or α_5 subunit;
- c) measuring *in vivo* effects of each compound in an animal model indicative of anxiolytic activity;
- d) measuring *in vivo* effects of each compound in an animal model indicative of sedative effects; and
- e) selecting each compound having: EC₅₀ values measured in a) of less than 200nM, efficacy values measured in a) greater than the efficacy measured in step b), a statistically significant ($p < 0.05$) positive effect in the animal model indicative of anxiolytic activity, and no statistically significant effect in the animal indicative of sedative effects.

Claim 55. (new) The method of claim 35, comprising:

- a) selecting a compound having a binding affinity less than 100 nM at any GABA_A receptor;
- b) measuring *in vitro* efficacy and EC₅₀ values for each selected compound at an $\alpha_2\beta_3\gamma_2$ and an $\alpha_3\beta_3\gamma_2$ GABA_A receptor;
- c) measuring *in vitro* efficacy for each selected compound at a GABA_A receptor comprised of an α_1 or α_5 subunit;
- d) measuring *in vivo* effects of each selected compound in an animal model indicative of anxiolytic activity;
- e) measuring *in vivo* effect of each selected compound in an animal model indicative of sedative effects; and
- f) selecting a compound having: EC₅₀ values measured in b) of less than 200nM, an efficacy measured in b) greater than the efficacy measured in c), a statistically significant ($p < 0.05$) positive effect in the animal model indicative of anxiolytic activity, and no statistically significant effect in the animal indicative of sedative effects.